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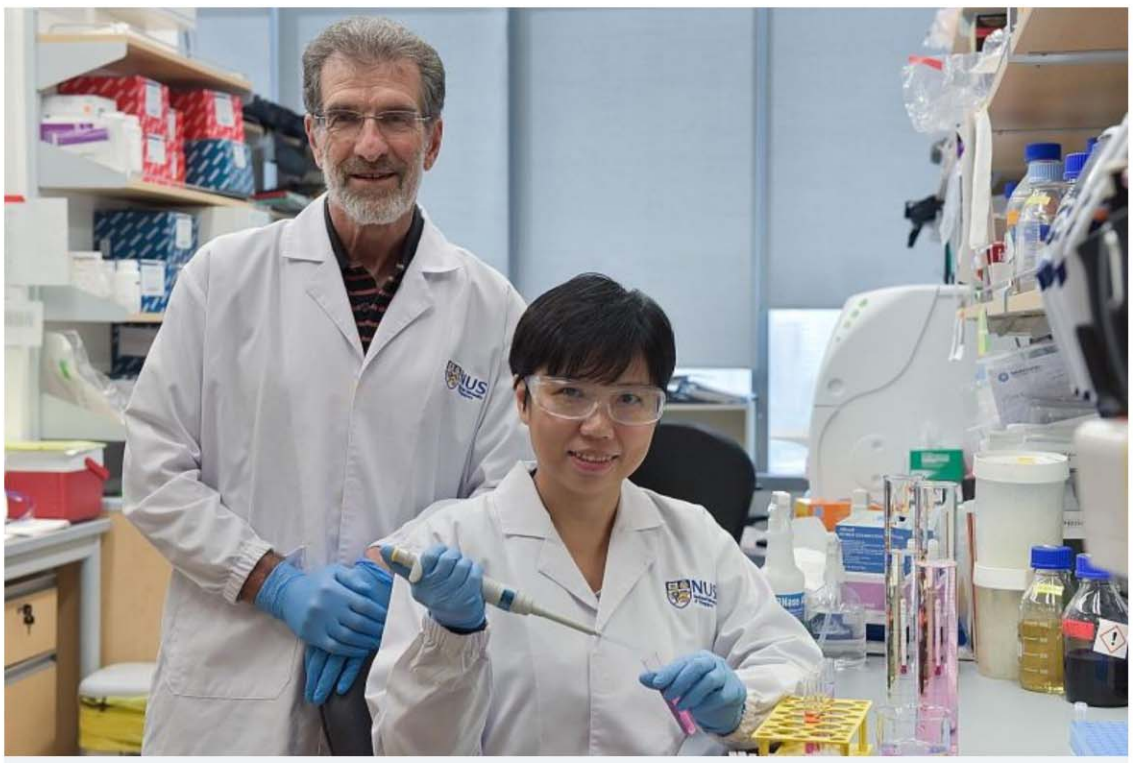
PREMIUM

Scientists find new drug that kills liver cancer cells



Professor Daniel Tenen and Dr Liu Bee Hui of the Cancer Science Institute of Singapore have designed a molecule to block the interaction between two proteins linked to cancer growth. PHOTO: LEE JIA WEN

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Drug created by the team mimics body's biological structures and has no significant side effects

Linette Lai Health Correspondent

Driving the growth of many cancerous tumours is a protein known as SALL4, which has been classified as an "undruggable target".

But scientists from the National University of Singapore (NUS) and Harvard Medical School believe they have found a solution in a new drug.

In about a third of cancers, SALL4 attaches to DNA in the cells and unleashes a cascade of activity that helps the cancer grow, so conventional drugs have nowhere to attach to on its surface and have no effect on it.

But unlike many cancer drugs which are constructed from chemical compounds, the drug created by the team more closely mimics biological structures in the body.

The researchers capitalised on the fact that SALL4 needs to interact with other proteins in order to work. First, they analysed its structure when it was bound to one of these other proteins, RBBp4.

Then they engineered a molecule with a stronger ability to bind to SALL4, effectively out-competing RBBp4.

When tested in the laboratory, liver tumour cells exposed to the drug became less active and died.

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NEW FRONTIER

The breakthrough in this study opens up a new therapeutic target where cancer control can be effected through regulation of genes, disrupting cancer growth while potentially avoiding the problems of chemotherapy resistance.

ASSOCIATE PROFESSOR DAN YOCK YOUNG, a senior consultant with the National University Hospital's gastroenterology and hepatology division, on the new drug treatment for liver cancer.

Regular cells however, were not affected, said Dr Liu Bee Hui, a research fellow at the Cancer Science Institute of Singapore at NUS.

This is an indication that those taking the drug will not experience significant side effects - which cannot be said of other cancer treatments such as chemotherapy.

Many chemotherapy drugs are designed to attack cells that are dividing quickly, explained Professor Daniel Tenen, who is director of the cancer institute. So they also attack rapidly growing cells such as hair follicles, which explains why patients can lose their hair.

"But cancer cells tend not to divide as fast as some normal cells - for example, hair cells. Cancer cells are often dividing more slowly than some normal cells, but they lack proper control of when to divide."

Liver cancer is one of the most common cancers among men in Singapore, and also a leading cause of death in this group.

Between 2011 and 2015, more than 2,500 people - mostly men - succumbed to the disease. As a general rule, patients typically survive less than a year after being diagnosed.

The new drug is believed to be effective against the most common form of liver cancer, known as hepatocellular carcinoma (HCC).

Researchers hope to use it with the current mainstay of treatment, another drug known as Sorafenib. Sorafenib is the first line of defence against liver cancer but has significant side effects, a limited impact on survival rates, and does not work on many people.

Before the new drug can be used in clinics, however, researchers need to learn the best way to administer it to patients.

It will also have to go through trials before it is used clinically.

Although the drug was tested only against liver cancer cells, the researchers believe that it has potential to be used alongside standard treatments against other cancers in which SALL4 plays a role - such as leukaemia, lung cancer and colon cancer.

This multi-pronged approach will hopefully give patients a better chance of beating cancer.

"It is unlikely to cure a malignant solid tumour, with many mutations activating multiple pathways, with just one drug," Prof Tenen said. "You will want to use multiple drugs that attack different pathways."

Professor Pierce Chow, who is a senior consultant at the National Cancer Centre Singapore's surgical oncology division, said that the researchers' work is "very promising".

Prof Chow, who is a clinician scientist - that is, a doctor who also does research - added that there are not many drugs effective against HCC.

"Although there is a new class of immunology drugs which are useful for patients with HCC, good response is still limited to around 20 per cent of patients," he said.

Associate Professor Dan Yock Young, a senior consultant with the National University Hospital's gastroenterology and hepatology division, said: "The breakthrough in this study opens up a new therapeutic target where cancer control can be effected through regulation of genes, disrupting cancer growth while potentially avoiding the problems of chemotherapy resistance."

Note: This story has been edited for clarity.

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